Applicant: Aladar A. Szalay et al. Attorney Docket No.: 3800002,00055 / 4804US

Serial No.: 10/516,785

Amendment after Final Filed : June 27, 2005

## AMENDMENTS TO THE CLAIMS:

Please amend claims 1, 6, 14, 16 and 21, and add claims 24-31 as follows. This listing of claims replaces all prior versions, and listings of claims, in the application.

## LISTING OF CLAIMS:

(Currently Amended) A method for diagnosis by detecting imaging wounded 1. or inflamed tissue inside of a <u>live</u> subject, comprising:

identifying a subject suspected of having an internal wound or inflammation to be tested for the presence or absence of internal wounded tissue or internal inflamed tissue therein;

systemically administering to the subject in whom the presence or absence of a wounded tissue or inflamed tissue is to be detected, a bacterium, wherein:

the bacterium encodes a protein that is detectable by imaging in the subject or encodes a protein that induces a signal detectable by imaging;

the bacterium replicates in the subject;

the bacterium is not pathogenic to the subject and is recognized by the immune system of the subject;

the bacterium is not targeted; and

after a sufficient time for the bacterium to accumulate in wounded or inflamed tissues inside of the subject, imaging the detectable bacterium inside of the live subject to detect accumulation of the bacterium in the subject, and thereby detecting imaging wounded or inflamed tissues inside of the live subject, wherein detection of imaging the accumulation indicates the location of wounded tissue or inflamed tissue inside of the subject.

- 2. (Currently Amended) The method of claim 1, wherein the bacterium encodes a protein(s) for the therapy of the detected imaged wounded or inflamed tissue.
- 3. (Withdrawn) The method of claim 1, wherein the bacterium encodes a luminescent or fluorescent protein.
- (Withdrawn) The method of claim 1, wherein the bacterium encodes a luciferase, red fluorescent protein or green fluorescent protein.
- (Withdrawn) The method of claim 4, wherein the bacterium encodes a luciferase and a protein(s) for the production of a substrate for a luciferase.
- (Currently Amended) A method for detecting wounded or inflamed tissue 6. inside a subject, comprising:

Applicant: Aladar A. Szalay et al. Attorney Docket No.: 3800002.00055 / 4804US Amendment after Final

Serial No.: 10/516,785

Filed : June 27, 2005

identifying a subject to be tested for the presence or absence of wounded tissue or inflamed tissue therein;

systemically administering to the subject in whom the presence or absence of a wounded tissue or inflamed tissue is to be detected, a bacterium, wherein:

the bacterium is detectable by imaging in the subject;

the bacterium replicates in the subject;

the bacterium is not pathogenic to the subject and is recognized by the immune system of the subject;

the bacterium is not targeted; and

after a sufficient time for the bacterium to accumulate in wounded or inflamed tissues inside of the subject, imaging the detectable bacterium inside of the subject to detect accumulation of the bacterium in the subject, and thereby detecting wounded or inflamed tissues inside of the subject, wherein:

detection of the accumulation indicates the location of wounded tissue or inflamed tissue inside of the subject; and The method of claim 1, wherein

the bacterium encodes a protein that induces a signal detectable by magnetic resonance imaging (MRI) or that binds to contrasting agent, chromophore or a ligand.

- 7. (Cancelled).
- 8. (Cancelled).
- 9. (Previously Presented) The method of claim 1, wherein the bacterium is selected among an attenuated Salmonella typhimurium, an attenuated Vibrio cholerae, an attenuated Listeria monocytogenes and E. coli.
  - 10. (Cancelled).
  - 11. (Cancelled).
- (Previously presented) The method of claim 2, wherein the protein for the 12. therapy is an enzyme that causes cell death or an enzyme that causes the digestion of debris.
- (Withdrawn) The method of claim 2, wherein the subject in whom the 13. presence or absence of wounded tissue or inflamed tissue is detected has a disease selected among endocarditis, pericarditis, inflammatory bowel disease, low back pain (herniated nucleus pulposis), temporal arteritis, polyarteritis nodosa and an arthritic disease.
- 14. (Currently Amended) The method of claim 2, wherein A method for detecting wounded or inflamed tissue inside of a subject, comprising:

Attorney Docket No.: 3800002.00055 / 4804US Applicant: Aladar A. Szalay et al. Amendment after Final

Serial No.: 10/516,785

Filed : June 27, 2005

identifying a subject to be tested for the presence or absence of wounded tissue or inflamed tissue therein;

systemically administering to the subject in whom the presence or absence of a wounded tissue or inflamed tissue is to be detected, a bacterium, wherein:

the bacterium is detectable by imaging in the subject;

the bacterium replicates in the subject;

the bacterium is not pathogenic to the subject and is recognized by the immune system of the subject;

the bacterium is not targeted; and

after a sufficient time for the bacterium to accumulate in wounded or inflamed tissues inside of the subject, imaging the detectable bacterium inside of the subject to detect accumulation of the bacterium in the subject, and thereby detecting wounded or inflamed tissues inside of the subject, wherein:

detection of the accumulation indicates the location of wounded tissue or inflamed tissue inside of the subject;

the bacterium encodes a protein(s) for the therapy of the detected imaged wounded or inflamed tissue; and

the subject for whom the presence or absence of wounded tissue or inflamed tissue is detected has an atherosclerotic disease.

- (Withdrawn) The method of claim 2, wherein the subject for whom the 15. presence or absence of wounded tissue or inflamed tissue is detected has a disease that is selected among coronary artery disease, peripheral vascular disease and cerebral artery disease.
- (Currently Amended) A method for detecting wounded or inflamed tissue 16. inside of a subject, comprising:

identifying a subject to be tested for the presence or absence of wounded tissue or inflamed tissue therein;

systemically administering to the subject in whom the presence or absence of a wounded tissue or inflamed tissue is to be detected, a bacterium, wherein:

the bacterium is detectable by imaging in the subject;

the bacterium replicates in the subject;

the bacterium is not pathogenic to the subject and is recognized by the immune system of the subject;

Attorney Docket No.: 3800002.00055 / 4804US Applicant: Aladar A. Szalay et al. Amendment after Final

Serial No.: 10/516,785

Filed : June 27, 2005

## the bacterium is not targeted; and

after a sufficient time for the bacterium to accumulate in wounded or inflamed tissues inside of the subject, imaging the detectable bacterium inside of the subject to detect accumulation of the bacterium in the subject, and thereby detecting wounded or inflamed tissues inside of the subject, wherein:

detection of the accumulation indicates the location of wounded tissue or inflamed tissue inside of the subject; and

The method of claim 1, wherein the monitoring detecting is performed by magnetic resonance imaging (MRI).

- 17. (Cancelled).
- (Previously presented) The method of claim 2, wherein the bacterium 18. contains an inducible promoter that regulates the expression of the therapeutic protein.
  - 19. (Cancelled).
  - 20. (Cancelled).
- (Currently Amended) The method of claim 2, wherein: A method for detecting 21. wounded or inflamed tissue inside of a subject, comprising:

identifying a subject to be tested for the presence or absence of wounded tissue or inflamed tissue therein;

systemically administering to the subject in whom the presence or absence of a wounded tissue or inflamed tissue is to be detected, a bacterium, wherein:

the bacterium is detectable by imaging in the subject;

the bacterium replicates in the subject;

the bacterium is not pathogenic to the subject and is recognized by the immune system of the subject;

the bacterium is not targeted; and

after a sufficient time for the bacterium to accumulate in wounded or inflamed tissues inside of the subject, imaging the detectable bacterium inside of the subject to detect accumulation of the bacterium in the subject, and thereby detecting wounded or inflamed tissues inside of the subject, wherein:

detection of the accumulation indicates the location of wounded tissue or inflamed tissue inside of the subject;

the disease is an atherosclerotic disease; and

Applicant: Aladar A. Szalay et al.

Attorney Docket No.: 3800002.00055 / 4804US

Serial No.: 10/516,785

Amendment after Final

Serial No.: 10/516,785 Filed: June 27, 2005

the therapeutic protein is selected from among a lipase, protease, lysozyme, proapoptotic factor and PPAR-agonist.

22. (Previously presented) The method of claim 1, further comprising: administering a therapeutic agent for the therapy of a wounded tissue, inflamed tissue or a disease associated therewith.

23. (Previously presented) A method for detecting wounded or inflamed tissue inside of a subject, comprising:

intravenously or intramuscularly administering to a subject in whom the presence or absence of a wounded tissue or inflamed tissue is to be detected, a bacterium, wherein:

the bacterium is detectable in the subject;

the bacterium replicates in the subject;

the bacterium is not pathogenic to the subject and is recognized by the immune system of the subject;

the bacterium is not targeted; and

after a sufficient time for the bacterium to accumulate in wounded or inflamed tissues inside of the subject, monitoring or imaging the detectable bacterium inside of the subject to detect accumulation of the bacterium in the subject, and thereby detecting wounded or inflamed tissues inside of the subject.

24. (New) The method of claim 23, further comprising:

administering a therapeutic agent for the therapy of a wounded tissue, inflamed tissue or a disease associated therewith.

- 25. (New) The method of claim 23, wherein the bacterium is selected among an attenuated *Salmonella typhimurium*, an attenuated *Vibrio cholerae*, an attenuated *Listeria monocytogenes* and *E. coli*.
- 26. (New) The method of claim 23, wherein the bacterium encodes a protein(s) for the therapy of the detected wounded or inflamed tissue.
- 27. (New, Withdrawn) The method of claim 23, wherein the bacterium encodes a luminescent or fluorescent protein.
- 28. (New, Withdrawn) The method of claim 23, wherein the bacterium encodes a luciferase, red fluorescent protein or green fluorescent protein.
- 29. (New, Withdrawn) The method of claim 28, wherein the bacterium encodes a luciferase and a protein(s) for the production of a substrate for a luciferase.

Applicant: Aladar A. Szalay et al. Attorney Docket No.: 3800002.00055 / 4804US Amendment after Final

Serial No.: 10/516,785

Filed : June 27, 2005

30. (New) The method of claim 24, wherein the protein for the therapy is an enzyme that causes cell death or an enzyme that causes the digestion of debris.

31. (New, Withdrawn) The method of claim 24, wherein the subject in whom the presence or absence of wounded tissue or inflamed tissue is detected has a disease selected among endocarditis, pericarditis, inflammatory bowel disease, low back pain (herniated nucleus pulposis), temporal arteritis, polyarteritis nodosa and an arthritic disease..